Reviewer's report

Title: Validity of Electron Beam Computed Tomography for Coronary Artery Disease: A Systematic Review and Meta-analysis

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Reviewer: Brahmajee Nallamothu

Reviewer's report:

General

Dendukuri et al performed an updated systematic review and meta-analysis of coronary calcification detection with electron-beam computed tomography (EBCT) for the detection of coronary artery disease (CAD) in asymptomatic and symptomatic patients. They found that higher EBCT scores indicated higher CAD risk in both symptomatic and asymptomatic populations, leading to implications for the management of both types of patients. Overall, these results are consistent with findings from earlier meta-analyses. The paper is important and will be of interest to readers of BMC. It is very well-written and the selection of studies is clearly articulated by the authors. The tables and figures also complement the text nicely.

Major Compulsory Revisions (that the author must respond to before a decision on publication can be reached)

1. The authors correctly point out that coronary artery calcification scores need to be interpreted in light of age- and gender-predicted values and few studies report such stratified values. They also mention the inability of their analysis to comment on the utility of EBCT scores beyond traditional risk factors which also implies for the management of patients. For these reasons, we believe that the authors should consider tempering their conclusions somewhat. In the Abstract, for example, their conclusions for asymptomatic patients in the High category and symptomatic patients in the Low category seem too firm (despite the qualifying phrase “can perhaps”). The authors themselves point out in the discussion that their results should not be used for “individual risk stratification” but reflect differences between populations.

2. The authors suggest directions for future EBCT research in the discussion. We agree with all these points. However, we recommend that the authors also mention the role of MDCT (at least briefly). MDCT has become a key tool for assessing coronary artery calcification scores in real world settings, essentially supplanting EBCT which is still restricted to a few research centers. Much additional research on coronary artery calcification will be performed with MDCT, which should be acknowledged in the paper.

3. This study compared the ratios of positive predictive value (PPV) and negative
predictive values (NPV) between groups. We understand the statistical reasons for pooling results in this manner but worry about its interpretability for clinicians. What exactly does it mean that “a symptomatic subject with a Low score has approximately one quarter the risk of having significant angiographic coronary stenosis than the Moderate/High categories”? Wouldn’t it be valuable to place these findings in the context of their absolute risk of an event? Also, how should we interpret the finding that the ratios of negative predictive values were consistent across risk categories of asymptomatic patients? Couldn’t the negative predictive values all be “similar” but inadequate?

Minor Essential Revisions (such as missing labels on figures, or the wrong use of a term, which the author can be trusted to correct)

4. The authors write that “among symptomatic patients, those with EBCT scores in the low category can perhaps, at least temporarily, avoid invasive coronary angiography.” We are somewhat concerned with this statement. Symptoms used for inclusion in the various studies that were considered for this paper are not clearly defined. In patients with unstable or high-risk symptoms, urgent cardiac catheterization may be indicated despite the findings of the EBCT (or other clinical tools), especially since vulnerable and ruptured plaques may be associated with little or no coronary calcium. This issue is strongly related to Point 1 above, which also cautions about patient-level recommendations based on these findings.

Discretionary Revisions (which the author can choose to ignore)

1. For Tables 1 and 2, couldn’t much of the “value” column be eliminated with individual cells directly reporting “yes,” “no”, and “NR” (not reported)? This may make the Tables easier to read.

2. Figure 2 demonstrates the low PPVs and significant overlap between moderate and high risk categories in asymptomatic patients. This may deserve more mention in the discussion.

Which journal?: Appropriate or potentially appropriate for BMC Medicine: an article of importance in its field

What next?: Unable to decide on acceptance or rejection until the authors have responded to the major compulsory revisions

Quality of written English: Acceptable

Statistical review: No

Declaration of competing interests:
I declare that I and Dr. LaBounty (who assisted with this review) have no competing interests.